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EXAMINER	
STARSIAK, JOHN S	

ART UNIT	PAPER NUMBER
1753	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/636,104	WANG ET AL.	
	Examiner	Art Unit	
	John S. Starsiak Jr.	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-71* is/are pending in the application.

4a) Of the above claim(s) *53-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33,35,42,46-52 and 68-71* is/are rejected.

7)☒ Claim(s) *34,36-38,40,41 and 43-45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Drawings

The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, 1) the "structure external to the chip" wherein the structure produces a "magnetic force" recited in claims 19, 21, 22, and 29; 2) the "structure external to the chip" wherein the structure produces an "electrostatic force" recited in claims 19, 25, 29, and 49; 3) the "structure external to the chip" wherein the structure produces a "mechanical force" recited in claims 19, 26, 29, and 49; 4) the "structure external to the chip" wherein the structure produces an "optical radiation force" recited in claims 19, 27, 29, and 49; 5) the "structure external to the chip" wherein the structure produces a "thermal convention force" recited in claim 19 must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-12, 19-27, 29 and 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 8 recites, "wherein the binding partner is selected from the group consisting of a cell, a cellular organelle, a virus, a microparticle, an aggregate or complex of molecules and an aggregate or complex thereof". While there is a recitation which corresponds to this claim in the written description of the invention, the only binding partner described in any detail is "a microparticle". Claim 19 recites, "wherein the physical force is selected from the group consisting of a dielectrophoresis, a traveling-wave dielectrophoresis, a magnetic, an acoustic, an electrostatic, a mechanical, an optical radiation force and a thermal convection force.". Claims 29 and 49 contain a similar recitation. While there is a recitation in the written description of the invention which corresponds to this recitation and outlines embodiments of the invention based on mechanical, optical radiation force and thermal convection force, there is no detailed description (including figures) of the embodiments of the invention based upon mechanical force, optical radiation force, or thermal convection force. The remaining claims are rejected because they depend on at least one of the above claims

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30, 31, 47, 46, and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 30 and 70 recite, "a plurality of microunits". Claim 31 recites, "a single unit". These terms are not defined in the context of the present invention. MPEP 608.01 (o) states: "The meaning of every term used in any claim should be apparent from the descriptive portion of the specification with clear disclosure to its import, and in mechanical cases, it should be identified in the descriptive portion of the specification by reference to the drawing, designating the part or parts therein to which the term applies.". For example, it is unclear if the traveling wave dielectrophoresis embodiment of the invention is a single unit or a plurality of units. Claims 46 and 47 recite, "wherein the moiety to be manipulated is *substantially coupled* onto the surface of the binding partner" and "wherein the moiety to be manipulated is *completely coupled* onto the surface of the binding partner", respectively. The terms "substantially coupled" and "completely coupled" are relative terms which render the claims indefinite. The terms "substantially coupled" and "completely coupled" and not defined in the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would be reasonably appraised of the scope of the invention.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-32, 35, 39, 42, 46, 47, 50-52, 70 and 71 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Zhou et al.

Regarding the "coupling" step and the "manipulating" step recited in claims 1, 70, and 71, these steps read on Zhou et al. [col. 5, lines 30 to 42]: "The present invention further discloses methods for **manipulating** biomolecules/bioparticles, chemical reagent molecules, drug molecules or other molecules or particles with an electromagnetic biochip...For controlling and handling non-magnetic particles and/or biomolecules, these materials are first magnetically modified. For example, the molecules may be covalently attached or physically absorbed to the surface. The biomolecules may be may be proteins (e.g. antibodies, antigens, and receptors), nucleic acids (e.g. single stranded DNA or RNA) or other molecules such as lipids or carbohydrates." The limitation regarding "chip format" recited in claims 1, 70, and 71 reads on the micro-electromagnetic chip 10 of Zhou et al. The "structure that is built in the chip" recited in claims 1, 70, and 71 reads on "micro-electromagnetic units 25 and conductive traces 18 and 30 of Zhou et al. The "structure that is external to the chip" recited in claims 1, 70, and 71 and the "plurality of microunits" recited in claim 70 read on Zhou et al. [col. 12, lines 57-61]: "The conductive traces 18 and 30 of the micro-electromagnetic unit array are powered by a DC current source. Each individual magnetic unit of the micro-electromagnetic unit array is controlled by selectively energizing different conductive traces 18, 30.". The "plurality of said moieties" recited in claims 1, 50, 51, 70, and 71 reads on Zhou et al. [col. 19, lines 22-24]: "For example, a library of candidate drug compounds could be prepared as ligand molecules and localized at predetermined

locations on the functional layer 42.". The "molecule" recited in the Markush group of claim 2, the "organic molecule" recited in the Markush group of claim 5, and the "protein, oligonucleotide, etc." recited in the Markush group of claim 7 read on Zhou et al. [col. 5, lines 39-42]: "the biomolecules may be proteins (e.g. antibodies, antigens, and receptors), nucleic acids (e.g. single stranded DNA or RNA) or other molecules such as lipids or carbohydrates. Methods according to the present invention may be used for hybridization and detection for specific sequences of DNA molecules, for antibody/antigen binding interaction in application areas such as drug screening, bio/chemical (i.e. biochemical or chemical) process control, biochemical monitoring and clinical diagnosis.". Claim 3 further limits the "cell" recited in the Markush group of claim 2. Claim 4 further limits the "cellular organelle" recited the Markush group of claim 2. However, both of these claims read on Zhou et al. because they recite "a molecule". Claim 6 further limits the "inorganic molecule" recited in the Markush group of claim 5. This claim reads on Zhou et al. because the claim recites "an organic molecule". The "microparticle" recited in the Markush group of claim 8 and "magnetic bead" recited in the Markush group of claim 12 read on "paramagnetic beads 56" of Zhou et al. Claim 9 further limits the "cell" recited in the Markush group of claim 8. Claim 10 further the "cellular organelle" recited in the Markush group of claim 8. Claims 9 and 10 read on Zhou et al. because these claims recite "a microparticle". The size range of the microparticles recited in claim 11 reads on Zhou et al. [col. 5, lines 22-24]: "Magnetic particles or materials used with the present invention may be of different sizes ranging from nanometer dimensions to micrometer and even millimeter dimensions,". Claim 13

recites, "wherein the moiety is coupled to the surface of the binding partner directly or via a linker.". Claim 13 reads on Zhou et al. because the claim reads on all possible ways of linking the moiety to the binding partner. The "cleavable linker" recited in claims 14 and 17 read on Zhou et al. [col. 16, lines 50-52]: "As shown in FIG. 14, the ligand molecules 44 may be linked onto the paramagnetic bead 56 through a cleavable linker 54.". Claim 15 reads on Zhou et al. [col. 5, lines 37-39]: "For example, the molecules may be covalently attached or physically absorbed to the surface of the magnetic particles.". The limitation recited in claim 16 reads on Zhou et al. because any linkage must be either specific or non-specific. Claim 18 reads on Zhou et al. [col. 16, lines 60-62]: "The cleavable linkers 54 may be photocleavable, heat cleavable, enzyme cleavable or cleavable by a specific chemical reaction. The magnetic force recited in claim 19 reads on the magnetic force, $F_{magnetic}$, of Zhou et al. The ferromagnetic material recited in claim 21 reads on "magnetic core 26" of Zhou et al. The microelectromagnetic unit in claim 22 reads on "conductive traces 18 and 30" of Zhou et al. Claim 20 further limits the "dielectrophoretic force" recited in Markush group of claim 19. Claims 23 and 24 further limit the "acoustic force" recited in the Markush group of claim 19. Claim 25 further limits the "electrostatic force" recited in the Markush group of claim 19. Claim 26 further limits the "mechanical force" recited in the Markush group of claim 19. Claim 27 further limits the "optical radiation force" recited in the Markush group of claim 19. Claims 20 and 23 to 27 read on Zhou et al. because all of these claims recite "a magnetic force". Claim 28 reads on Zhou et al. [col. 6, lines 34-36]: "...substrate 16, which can be made of silicon, glass, silicon-oxide, plastics, ceramics,

or other solid or porous materials.". The "structure that is external to the chip" recited in claim 29 reads on the "DC current source" of Zhou et al. The "plurality of microunits" recited in claim 30 reads on the "individually addressable micro-electromagnetic units arrange in arrays" of Zhou et al. Claim 31 reads on Zhou et al. [col. 3, lines 46-48]: "An electromagnetic biochip may have a **single** or multiple microelectromagnetic unit arrays". Claim 32 reads on Zhou et al. [col. 16, lines 50-53]: "As shown in FIG.14, the ligand molecules 44 may be linked onto a paramagnetic bead 56 through a cleavable linker. Thus, the ligand molecules can be transported..." and Zhou et al. [col. 5, lines 46 and 47]: "...magnetic particles are concentrated at specific locations...". Claim 33 reads on Zhou et al. [col. 16, lines 52 and 53]: "Thus, the ligand molecules can be transported, manipulated, and **released** at specific regions...". Claims 35 and 39 read on Zhou et al. [col.5, lines 49-51]: "...binding between molecules (e.g, **antibody+antigen**; **specific DNA probe and its complementary single-stranded target DNA** ...". Claim 42 reads on Zhou et al. col. 5, lines 30 to 42, see rejection of claim 1 above. Since the written description fails specifically define what "substantially coupled" and "completely completed" mean in the context of the present invention claims 46 and 47 are considered to be inherent in the method of Zhou et al. Claim 52 reads on Zhou et al. because the manipulation of a plurality must either be sequential or simultaneous.

Claims 1-7, 13-25, 29, 31-33, 39, and 46-48 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Apffel et al.

Apffel et al. discloses a process, illustrated in FIG. 5 and described from line 40 of column 9 to line 5 of column 10, in which two species combine to form a single entity.

Apffel et al discloses that these two species can be an "analyte" and an "analyte-binding partner". The "moiety" and "binding partner" recited in claim 1 read on the "analyte" and "analyte-binding partner" of Apffel et al, respectively. Specifically, Apffel et al teaches [col. 3, lines 4-15]: "The terms "analyte" and "analyte sample" are used interchangeably herein to refer to one or *a mixture of molecules* (or portions thereof) whose mass is to be measured by the technique of MALDI-TOF MS...An analyte can be obtained from biological fluids, cell or tissue extracts, fermentation broths, food stuffs, microorganisms, viruses, plants, environmental materials and the like or may originate by synthetic, semi-synthetic, or other processes not found in nature (e.g., by combinatorial synthesis). Specifically, Apffel et al teaches [col. 3, lines 23-34]: "The terms "analyte-binding partner" or "analyte capture molecule" are used interchangeably herein to refer to molecules that recognize general physicochemical characteristics of the "target analyte" (e.g., hydrophobic domain or hydrophilic surface of the protein, strandedness of a nucleic acid) or specific chemical features (e.g., amino acids, sugars or nucleotide sequences). Binding partners may include binding proteins or portions thereof (e.g., binding proteins for receptors, hormones, vitamins, etc.), peptides, biomimetic molecules (e.g. flexible polymeric ion-exchangers), oligonucleotides and oligonucleotide analogs, lectins, and the like.". Hence, the "coupling" step recited in claim 1 reads on the above process of Apffel et al. The "manipulating" step of claim 1 reads on the final step of the above process of Apffel et al. (i.e., [col. 9, lines 65-67]): "The derivatized sample, AB, is then electrophoretically and/or electroosmotically moved to the MALDI ionization surface (panel (d))." . The "chip" format recited in claim 1 reads on the

"planar manifold 21" of Apffel et al. The "structure that is built-in to said chip" reads on the microchannel 25; reservoirs 27, 29, 31; MALDI ionization surface 33; and electrical connections 42, 44, 46, and 48 of Apffel et al. Although Apffel et al. does not explicitly describe any "structure that is external to the chip", it is inherent that in order to perform the process described by Apffel et al. that a controllable source of DC voltage must be connected to electrical connections 42, 44, 46, and 48 of Apffel et al. The "plurality of moieties" recited in claims 1 and 50; and the limitations recited in claims 51 and 52 read on Apffel et al. [col. 5, lines 47-53]: "A plurality of reaction zones may be provided within the sample handling compartment for carrying out simultaneous reactions under the same or different conditions, for successive chemical manipulations of an analyte...for analysis of complex analyte mixtures, and the like. Claim 2 reads on the list of analytes taught by Apffel et al. (e.g. virus). Claim 3 further limits the "cell" recited in the Markush group of claim 2. Claim 4 further limits the "cellular organelle" recited in the Markush group of claim 2. Claim 5 further limits the "molecule" recited in the Markush group of claim 2. Claim 6 further limits the "inorganic molecule" recited in the Markush group of claim 5, which further limits the "molecule" recited in the Markush group of claim 2. Claim 7 further limits the "organic molecule" recited in the Markush group of claim 5, which further limits the "molecule" recited in the Markush group of claim 2. Claims 3-7 read on Apffel et al. because they recite "a virus". Claim 13 reads on Apffel et al because the coupling between the "analyte" and the "analyte-binding partner" of Apffel et al. must either be direct or via a linker. Claim 15 reads on Apffel et al. because the coupling between the "analyte" and the "analyte-binding partner" of Apffel et al. must

either be covalent or non-covalent. Claim 16 reads on Apffel et al. because the coupling between the "analyte" and the "analyte-binding partner" of Apffel et al. must either specific or non-specific. Claims 14, 17, 18, and 33 which recite either the cleavability of the linkage between the "moiety and the binding partner" or the "decoupling of the "moiety" and the "binding partner" read on Apffel et al. [col.6, lines 43-48]: "A captured analyte may be released into the solution by various methods known in the art to dissociate high affinity binding mediated by hydrogen bonds, electrostatic, hydrophobic and polar interactions or combination thereof (e.g., changing temperature, pH, solvent polarity, using chaotropic salts, localized heating with laser irradiation, and the like).". Claims 19, 25, 29, and 49 read on Apffel et al. because although Apffel et al. does not explicitly "an electrostatic force", the electrophoresis/electroomosis recited in Apffel et al. corresponds to electrostatic because electrophoresis/electroosmosis require a DC electric field, i.e. claim 25 recites, "the electrostatic force is effected via a direct current (DC) electric field". Claim 20 further limits the "dielectrophoretic force" recited in the Markush group of claim 19. Claims 21 and 22 limit the "magnetic force" recited in the Markush group of claim 19. Claim 23 and 24 further limits the "acoustic force" recited in the Markush group of claim 19. Claim 26 further limits the "mechanical force" recited in the Markush group of claim 19. Claim 27 further limits the "optical radiation force" recited in the Markush group of claim 19. Claims 20-24, 26, and 27 read on Apffel et al. because all of the claims recite "an electrostatic force". Claim 31 reads on Apffel et al. because Apffel et al. discloses a single unit on the chip. The "transportation" recited in the Markush group of the claim 32 reads on the final step of the process of Apffel et al.

described above. Since the written description of the invention fails to clearly define the limitation intended by "substantially coupled" (claim 46), "completely coupled" (claim 47), and in particular the difference between "substantially coupled" and "completely coupled", claims 46 and 47 read on the coupling of Appfel et al. Claim 48 reads on Apffel et al. since the physical force in Appfel et al. is not a magnetic force.

Claims 1-7,13, 15, 16, 19-25, 28, 31, 32, 48, 50, 52, and 68 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Fuchs et al.

The "coupling" step recited in claim 1 reads on either the binding of the analyte to the first binding partner or the binding of the analyte to the second binding partner of Fuchs et al. Specifically, Fuchs et al teaches [col.2, lines 44-52]: "In one aspect, the present invention provides a method for electroseparation analysis of a mixture involving the step of electrically separating in a mixture containing: (1) a sample; (2) a first binding partner which binds to a first binding site on an analyte; and (3) a second binding partner which binds to a second binding site on the analyte, whereby first and second binding partners bind to the analyte, if present in the sample, to form a three-membered complex which is electrically separable from unbound first binding partner.". The "manipulating" step reads on the electroseparation of Fuchs et al. The chip recited in the "manipulating" step reads on the apparatus 10 of Fuchs et al. consisting of fused silica substrate 12 and second fused silica substrate 30. The "structure that is built-in said chip" recited in claim 1 reads on flow-through channel 20 and ports 16, 24, and 26 of Fuchs et al. The "structure that is external to said chip" recited in claim 1 reads on

the support structure of Fuchs et al. Specifically, Fuchs et al. teaches [col. 20, 61-63]: "During the analysis, the device 10 may be placed in a support structure with fluidic and electrical connections to the ports 16, 24, and 26.". Regarding the "plurality of moieties" recited in claims 1 and 50 this limitation reads on Fuchs et al. [col. 15, 44-50]: "The methods of the instant invention can be used to detect two or more different analytes in a sample. The skilled practitioner is able to choose among possible binding partners, detectable moieties, and charge-modifying moieties such that the presence, absence or concentration of two or more different analytes can be determined using the methods disclosed herein and routine experimentation.". Claims 2, 5, and 7 read on Fuchs et al. [col. 8, lines 17-22]: "Preferred analytes include...proteins, peptides, nucleic acids,...carbohydrates...". Claim 3 further limits the "cell" recited in the Markush group of claim 2. Claim 4 further limits the "cellular organelle" recited in the Markush group of claim 2. However, these claims recite "a molecule" which read on Fuchs et al. (e.g., a protein). Claim 6 further limits the "inorganic molecule" recited in the Markush group of claim 5. However, claim 6 recites "an organic molecule" which reads on Fuchs et al. (e.g., a protein). Claim 13 reads on Fuchs et al because the binding in Fuchs et al must either be "direct" or "via a linker". Claim 15 reads on Fuchs et al because the binding in Fuchs et al. must be either covalent or non-covalent. Claim 16 reads on Fuchs et al. because the binding in Fuchs et al. must be either specific or non-specific. Claims 19 and 29 recite, "the physical force is...electrostatic...". Claim 25 recites, "wherein the electrostatic force is effected via a direct current (DC) electric field". These claims read on Fuchs et al.because capillary electrophoresis utilizes a DC electric field. Claim 20

further limits the "dielectrophoresis force" and the "traveling wave dielectrophoresis force" recited in the Markush group of claim 19. Claim 21 and 22 further limit the "magnetic force" recited in the Markush group of claim 19. Claims 24 and 25 further limits the "acoustic force" recited in the Markush group of claim 19. Claim 26 further limits the "mechanical force" recited in the Markush group of claim 19. Claim 27 further limits the "optical radiation force" recited in the Markush group of claim 19. Claims 20-24, 26, and 27 read on Fuchs et al. because these claims recite an "electrostatic force". Claim 28 reads on Fuchs et al. [col. 20, lines 21-24]: "The apparatus of the invention for ultrafast electroseparation analysis can be designed and fabricated in large quantities from a solid substrate material. Silicon, silica, and glass are preferred...". Claim 31 reads on Fuchs et al because the device of Fuchs et al comprises a single unit. Both the "transportation" and the "separation" recited in the Markush group of claim 32 read on the electroseparation" of Fuchs et al. Claim 48 reads on Fuchs et al. because the physical force is not magnetic. Claim 52 reads on Fuchs et al. because the plurality of analytes of Fuchs et al. must be manipulated either sequentially or simultaneously. Claim 68 (a kit claim) reads on [col. 22, lines 38-43]: "In yet another aspect, the claimed invention provides kits for detecting the presence, absence, or concentration of an analyte using electroseparation analysis. Preferred embodiments of kits are configured to detect clinically relevant analytes in biological samples. In one embodiment, the kits of the present invention comprise reagents and apparatus.".

Claims 1-7, 13, 15, 16, 19, 26, 29, 49 and 50 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Wu et al.

The "coupling" step recited in claim 1 reads on Wu et al. [col. 6, lines 14-23]: "In the illustrated embodiment the reaction in channel 30 is a complex formation between antigen and antibody. The term "reaction" as used herein includes any interaction between the analyte particle and reagent particle which leads to a detectable change. It includes chemical reaction, physical binding, adsorption, absorption (for example when the analyte particle is sucked inside a porous reagent particle such as a zeolite), antibody reaction, nucleic acid binding, ion pairing, ion exchange, chromatographic type reaction and receptor hormone interaction." The "manipulating" step reads on the transport of the "complex" out of the H reactor into the T reactor of Wu et al. The "chip" and the "structure that is built-in in said chip" reads on Wu et al. [col. 11, line 65 – col. 12, line 8]: "In either the parallel or perpendicular embodiment, the channel cell is generally formed by two plates with abutting surfaces. The channels may be formed in both plates, or one plate can contain the channels and the other can be a flat cover plate. The channel cells of this invention may be formed by any techniques known in the art. Silicon channel plates are preferably formed by etching the flow channels onto the horizontal surface of the silicon microchip and placing a cover plate, preferably of an optically clear material such as glass or a silicon rubber sheet, on the etched substrate plate.". The " structure that is external to said chip" reads on Wu et al. [col. 12, lines 40-47]: "Means for applying pressure to the flow of the feed fluids through the device can be provided. Such means can be provided at the inlets and/or the outlets (e.g. as

vacuum exerted by chemical or mechanical means). Means for applying such pressure are known in the art, and include the use of a column of water or other means of applying water pressure, electroendoosmotic forces, optical forces, gravitational forces, and surface tension forces.". The "plurality of said moieties" recited in claims 1 and 50 read on Wu et al. [col. 6, line 62 – col.7, line 4]: "The reagent particles can be reporter immobilized on beads to form reporter beads 24, as shown in FIG. 3. Each reporter bead comprises a bead having a plurality of at least one type of reporter molecules immobilized thereon. A property of the reporter bead, such as fluorescence, luminescence, absorbance or chemical activity, is sensitive to the corresponding analyte. The use of reporter beads allows for a plurality of analytes to be measured simultaneously through a single reagent inlet because the beads can be tagged with different reporter molecules.". Claims 2, and 5 to 7 read on Wu et al. [col. 3, line 62 – col. 4, line 1]: "Examples of analyte particles are hydrogen, calcium, sodium and other ions, dissolved oxygen, proteins such as albumin, organic molecules such as alcohols and sugars, drugs such as salicylic acid, halothane and narcotics, pesticides, heavy metals, organic and inorganic polymers, viruses, small cells and other particles.". Claim 3 further limits the "cell" recited in the Markush group of claim 2. Claim 4 further limits "cellular organelle" recited in the Markush group of claim 2. However these claims read on Wu et al. because they recite a cell, a virus, and a molecule. Claim 13 read on Wu et al since the coupling in Wu et al. must be either direct or via a linker. Claim 15 reads on Wu et al. since the coupling in Wu et al. must either be covalent or non-covalent. Claim 16 reads on Wu et al. because the coupling in Wu et al must be either specific or

non-specific. Claims 19, 26, 29 and 49 read on Wu et al. because the physical force in Wu et al. is a mechanical force, i.e., fluid flow.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-13, 15, 16, 19-27, 29, 31, 32, 39, 46-50, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu.

Claim 1 reads on Liu except for the recited of a plurality of moieties. Specifically, the "coupling" step recited in claim 1 reads on Liu [col. 11, lines 9-11]: "In well 2, the capture antibodies affixed to the microbead bind antigen present in the serum sample." The "manipulating" step in claim 1 reads on Liu [col.11, lines 11-14]: "Next the microbead is transferred into well 3, where the captured antigen reacts with a labeled antibody (step $). In step 5, the microbead is transferred from well 3 into well 4, where it undergoes fluorescent detection...". Regarding the phrase "in a chip format" recited in claim 1, while Liu does not explicitly recited this phrase, it is considered to be inherent given the dimensions of the apparatus of Liu, e.g., "For example, in one preferred embodiment, a microchannel having a cross-sectional diameter of 10x10 μm^2 was found to be sufficient to allow the active movement of a 5-μm microbead...". Regarding the "structure that is built in said chip" recited in the "manipulating" step of claim 1, this

structure reads the wells (54, 58, 62, 66) and microchannel 70 of Liu. The "structure that is external to the chip" recited in the "manipulating" step of claim 1 reads on "microbead manipulation" portion 100 of the device of Liu. The recitation of "a plurality of said moieties is manipluated" is considered to include simply performing one of the processes described by Liu more than once. This interpretation is support by claim 52, i.e. "wherein the plurality of moieties is manipulated **sequentiall**y or simultaneously.". It would have been obvious to one of ordinary skill in the art at the time of the invention that any of the processes described by Liu could be performed repeatedly on a plurality of samples. The "molecule" recited in the Markush group of claim 2 reads on either the antigen or the antibody recited in Liu. Claim 3 further limits the "cell" recited in the Markush group of claim 2. Claim 4 further limits the "cellular organelle" recited in the Markush group of claim 2. However, both of these claims read on Liu because they recite "a molecule". The "organic molecule" in the Markush group of claim 15 reads on either the antigen or the antibody of Liu. Claim 6 further limits the inorganic molecule recited in the Markush group of claim 5. However, claim 6 reads on Liu because the claim recites "an organic molecule". The "protein" recited in the Markush group of claim 7 reads on the antibody of Liu because antibodies are proteins. The "microparticle" recited in the Markush group of claim 8 reads on the microbead(s) of Liu. Claim 9 further limits the "cell" recited the Markush group of claim 8. Claim 10 further limits the "cellular organelle" recited in the Markush group of claim 8. Claims 9 and 10 read on Liu because these claims recite "a protein". Claim 11 and 12 read on Liu [col. 9, lines 55-57]: "...the microbeads, preferably constructed of either glass or polystyrene, and

from about 0.1 micron to about 20 microns.". Claim 13 reads on Liu since any coupling in Liu must either be direct or via a linker. Claim 15 reads on Liu since any coupling in Liu is either covalent or non-covalent. Claim 16 reads on Liu since any binding in Liu is either specific or non-specific. The "optical radiation force" recited in the Markush groups of claims 19, 29, and 49 reads on the "optical tweezers" recited in Liu. Claim 27 (laser tweezers) read on Liu because the bead manipulation portion of Liu uses a YAG laser. Claim 20 further limits the "dielectrophoresis force" recited in the Markush group of claim 19. Claims 21 and 22 further limit the "magnetic force" recited in the Markush group of claim 19. Claims 23 and 24 further limit the "acoustic force" recited in the Markush group of claim 19. Claim 25 further limits the "mechanical force" recited in the Markush groups of claim 19. Claims 20-26 read on Liu since these claims recite a "optical radiation force". Claim 31 reads on Liu because it comprises a single unit. The "transportation" recited in the Markush group of claim 32 reads on the transportation between wells of Liu. Claim 39 read on Liu [col. 11, lines 9-11]: "In well 2, the capture antibodies affixed to the microbead binding antigen present in the serum sample.". Since the written description of the invention fails to clearly define the limitation intended by "substantially coupled" and "completely coupled" recited in claims 46 and 47, respectively and in particular the difference between these limitations, Liu reads on both of these claims. Claims 48 and 49 read on Liu since the force in Liu is an optical radiation force. Regarding claims 50 and 52 see details of the rejection of claim 1 above.

Claim 69 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fuchs et al.

All of the elements of the claimed "kit" are present in the kits(s) of Fuchs et al. except for instruction(s). Including instructions in kits is notoriously well-known. It would have been obvious to one of ordinary skill in the art at the time of the invention to include instruction (s) in the kit(s) of Fuchs et al. because instructions are necessary in order to use the kit.

Allowable Subject Matter

Claims 34, 36, 37, 38, 40, 41, and 43-45 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

Applicant's arguments filed 07 January 2004 have been fully considered but they are not persuasive.

Applicant's arguments directed to the objection to the drawings are not well-taken because while the figures illustrate the "structure external to the chip" (only as black boxes) for some of the claimed embodiments, the figures do not illustrate all of the claimed "structures external to the chip". In the present Action the examiner particularly

points out which "claimed embodiments" are not properly illustrated. Applicant's arguments directed to the rejections based on non-enablement are not well-taken for the following reasons. In his first argument the applicant refers the examiner to several portions of the written description, which he argues teach how to make and use the claimed invention. However, the portions of the written description are often unrelated to the subject matter which the applicant alleges it teaches. For example, the applicant argues that page 24, lines 1-9 teach "what types of binding partners, e.g. cells, cellular organelles and viruses, etc can be used". However, examination of this portion of the written description of the invention shows it to be unrelated to "cells, cellular organelles, and viruses". Similarly, page 24, lines 19-24, of the written description of the invention does not teach "selecting a binding partner". While page 26, line 24 to page 31, line 20 of the written description of the invent does teach a litany of coupling mechanisms and some specific example of binding mechanisms, which can be used when the binding partner is a microparticle, the portion of the written description is devoid of any teaching of which coupling mechanisms would be used when the binding partner is a cell, cell organelle, or a virus. While, page 31, line 22 to page 46, line 5 of the written description of the invention broadly teach using mechanical force, optical radiation force, and thermal convection force as the physical force in the present invention and there is some limited discussion of the structure the thermal convection and the optical radiation embodiments of the present invention, this portion fails to sufficiently describe the structure of the chip for the thermal convection and optical radiation embodiments of the present invention and is totally devoid of any structure of the mechanical embodiment of

the present invention. Similarly, page 40, line 9 to page 41, line 32, of the written description contains limited disclosure of the thermal convection and optical radiation embodiments; and is devoid of discussion of the mechanical embodiment. In his second argument regarding the rejections based on lack of enablement the applicant alleges "one skilled in the art could make and use the claimed invention". The applicant appears to be arguing that the *knowledge* of one skilled in the art together with the written description renders the claims enabling. However, the applicant fails to specifically point out what those teachings are is and to demonstrate that these teachings are known in the art. The examiner believes it is well-established that when a written description relies on what is known in the art for enablement that the applicant must positively demonstrate that the subject matter is known in the art. Regarding the rejection of claim 30 and 31 based on 35 USC 112, 2nd paragraph, the applicant refers the examiner to several portions of the written description. However, in none of the portions are the terms " plurality of microunits" or "single microunit" defined or even used. Applicant's argument directed the rejection of claims 46 and 47 since the applicant fails to shown how the written description of the invention gives definiteness to the terms "substantially coupled" and "completely coupled". In one of the cases actually cited by the applicant the court held "*substantially*...was definite in view of the guidelines contained in the specification". Applicant's arguments directed to the art rejections are moot in view of the new grounds of rejection.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Starsiak Jr. whose telephone number is (571) 272-1346. The examiner can normally be reached on Monday to Friday from 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NAM NGUYEN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1700

John S. Starsiak Jr.

29 April 2004